

Online Research @ Cardiff

This is an Open Access document downloaded from ORCA, Cardiff University's institutional repository: <https://orca.cardiff.ac.uk/id/eprint/108760/>

This is the author's version of a work that was submitted to / accepted for publication.

Citation for final published version:

Al-Kadhim, Karrar A. H., Pritchard, Manon ORCID: <https://orcid.org/0000-0002-5135-4744>, Farnell, Damian ORCID: <https://orcid.org/0000-0003-0662-1927>, Thomas, David W. ORCID: <https://orcid.org/0000-0001-7319-5820>, Adams, Robert and Claydon, Nicholas ORCID: <https://orcid.org/0000-0002-4151-1515> 2018. Surgical therapy for peri-implantitis management: a systematic review and meta-analysis. Oral Surgery 11 (3) , pp. 200-212. 10.1111/ors.12344 file

Publishers page: <http://dx.doi.org/10.1111/ors.12344>
<<http://dx.doi.org/10.1111/ors.12344>>

Please note:

Changes made as a result of publishing processes such as copy-editing, formatting and page numbers may not be reflected in this version. For the definitive version of this publication, please refer to the published source. You are advised to consult the publisher's version if you wish to cite this paper.

This version is being made available in accordance with publisher policies.

See

<http://orca.cf.ac.uk/policies.html> for usage policies. Copyright and moral rights for publications made available in ORCA are retained by the copyright holders.



Surgical therapy for peri-implantitis management: a systematic review and meta-analysis

Abbreviated running title: Surgical peri-implantitis management

Karrar A. H. Al-Kadhim¹, Manon F. Pritchard^{1*}, Damian J. J. Farnell¹, David W. Thomas¹, Robert Adams¹, Nicholas Claydon¹

¹Cardiff University, School of Dentistry, Heath Park, Cardiff, UK. CF14 4XY.

Corresponding author: Dr Manon Prichard, Advanced Therapies Group, Cardiff University, School of Dentistry, Heath Park, Cardiff, UK. E-mail: pritchardmf@cardiff.ac.uk

Conflict of Interest: The authors have no conflict of interest

Author contribution: The concept and design of the study was by N.C, R.A, and D.W.T. Data analysis and interpretation was by K.A.K, D.F, N.C and D.W.T. Drafting of the article and critical revision was by M.F.P, N.C, R.A, and D.W.T. Approval of article was obtained by all authors. Statistics was carried out by D.F and K.A.K. Data collection was by K.A.K.

Keyword: dental implants, osseointegration, meta-analysis, systematic review

Abstract

Aim: Peri-implantitis is a common cause of late implant failure. Studies have investigated different treatment strategies. The effectiveness of these modalities, however, remains unclear. This study aimed to evaluate the success of surgical peri-implantitis treatment using clinical and radiographic parameters.

Material and methods: A systematic review of published literature was employed. Key words were selected to conduct an electronic search using four databases for literature on human clinical studies. Meta-analyses were carried out for clinical probing, pocket depth and radiographic bone level.

Results: A total of 16 papers met the inclusion criteria. Four treatment modalities to supplement mechanical debridement were identified: 1) apically-repositioned flap, 2) chemical surface decontamination, 3) implantoplasty and, 4) bone augmentation. Inconsistent results were evident which were dependent on several treatment-independent factors. No clinical benefits were identified for the additional use of surface decontamination, while limited evidence demonstrated improvement of clinical and radiographic outcomes after implantoplasty. The effect of bone augmentation appeared limited to 'filling' radiographic defects.

Conclusions: The outcomes of the currently available surgical interventions for peri-implantitis remain unpredictable. There is no reliable evidence to suggest which methods are the most effective. Further randomised-controlled studies are needed to identify the best treatment methods.

Clinical Relevance

Scientific rationale for study: In the management of patients with peri-implantitis, the treatment of established bony defects around fixtures remains a significant clinical challenge. Principal findings: Whilst a range of surgical treatment modalities have been described, from simple debridement to implantoplasty and attempted guided-tissue regeneration, the individual techniques employed often appear based on operator-preference. Practical implications: This systematic review sought to evaluate the existing evidence to compare the existing surgical treatment modalities, determine their effectiveness and inform the management of these patients, however, the outcomes remain unpredictable. Further studies are required to discover the optimal surgical treatment approach for peri-implantitis.

Introduction

Implants provide a long-term, generally predictable treatment to restore function¹, aesthetics², self-esteem³, and quality of life⁴ following tooth-loss. The application and use of dental implants has increased and now represents an indispensable therapeutic option for the replacement of missing teeth.

Peri-implantitis is considered to be the main biological cause of 5-year implant failure^{5,6}. Review studies have estimated that peri-implantitis will affect 28%-56% of patients and 12%–43% of individual implant sites^{7,8}. This variation in prevalence may reflect differences in study design, population size and risk profiles, and the clinical ‘definition’ of peri-implantitis^{7,9}. There remains a lack of evidence regarding treatment and prognosis of peri-implantitis⁸.

The inflammatory destruction of peri-implant tissue is multi-factorial. However, biofilm and bacterial infection are considered to be the major aetiological features in the development of peri-implant disease⁸. Smoking is also a strong predictor of implant failure¹⁰, leading to an increase in prevalence that is 4.7 times greater than is observed in non-smokers¹¹. Implant failure is 6 times greater in patients with a history of periodontitis than those who did not have a history of

periodontitis¹¹. Systemic risk factors such as diabetes, cardiovascular diseases, age, gender, and genetics have been suggested as potential risk factors, although studies are limited^{12,13}. Local risk factors, e.g. excess cement, was associated with signs of peri-implantitis in 100% of patient with a history of periodontal disease and 65% of healthy controls¹⁴.

The diagnosis of peri-implantitis depends on the presence of inflammatory signs, bleeding on probing (BOP) or suppuration on probing (SOP) and the degree of bone loss evident radiographically¹⁵. However, it is important to distinguish this diagnosis of peri-implantitis from bone resorption resulting from bone remodelling which occurs early after implant placement⁷. Some authors do not consider peri-implantitis as a differential diagnosis unless the implants have been in place for >12 months¹⁶⁻¹⁸.

The consensus report of the 11th *European Workshop on Periodontology* highlights steps to reduce the risk of incidence of peri-implantitis¹⁹. The indications for appropriate management strategies that appear in clinical studies have resulted in development of the 'cumulative interceptive supportive therapy'^{15, 20, 21}. The management of peri-implantitis is based on similar techniques to those of periodontitis¹¹ which entail the elimination of inflammation and prevention of further bone loss; including non-surgical (conventional) and surgical treatment²². Conventional non-surgical treatment can be classified into mechanical, chemical and light-mediated therapies. Reviews and meta-analyses have concluded that there is no reliable non-surgical treatment which results in elimination of the disease²³⁻²⁵.

Surgical treatment allows better access to the implant surface and the surrounding bony defect²⁶ and is used in conjunction with patient-directed care, and non-surgical therapy to reduce bacterial colonization and local inflammation²¹. Mechanical debridement of the implant surface can be achieved using curettes, ultrasonic scalers, or air-abrasion, in the presence or absence of systemic antibiotics. A 3-month follow-up study has shown that mechanical debridement alone, following surgical access, is effective in reducing clinical/microbial parameters²⁷. Whilst adjunctive surface decontamination with antimicrobials such as chlorhexidine (CHX) reduced microbial counts, this had

no significant effect on clinical or radiographic parameters^{28, 29}. Leonhardt et al. (2003) reported that significant reduction in BOP and PPD (periodontal probing depth) following surgical debridement and decontamination with H₂O₂³⁰. Although many clinicians employ topical antibiotics e.g. tetracycline and minocycline, their clinical effect remains unclear³¹.

Lasers have been shown to have no additional clinical benefit as a potential surface-decontamination agents during surgical therapy when compared with mechanical debridement^{32, 33}. Photo-dynamic therapy (PDT) was shown to significantly decrease BOP and PPD between test and control subjects in a randomised control trials (RCT), although the bacterial counts showed no difference between the two groups³⁴.

Adjunctive resective surgery using osteoplasty, with or without apically re-positioned flap (ARF) procedures, has been reported to improve clinical sign of peri-implantitis, where PPD ≥ 6 mm were eliminated in 77% of subjects³⁵. However, the use of ARF in the aesthetic zone is limited¹¹. Implantoplasty is directed to reduce surface-roughness of the implant surface to decrease bacterial and biofilm accumulation³⁶. However, concerns have been raised regarding the reduction of implant strength³⁷, deposits of titanium particles in the soft- and hard-tissues³⁸ and increased marginal tissue recession and exposure of the implant surface³¹. Re-osseointegration using bone augmentation (autogenous bone^{39,40} and/or synthetic bone graft materials^{41,42} may provide a significant improvement in clinical and radiographic parameters compared to the baseline. Bone graft (autogenous or synthetic), however, cannot be integrated on to a metal surface⁴³. Furthermore, it has been shown that the use of membrane/s with autogenous or synthetic materials has no additional benefit^{40, 44}.

The aim of this systematic review was to critically evaluate the current literature on the surgical treatment of peri-implantitis and assess the effectiveness of treatment modalities (and adjunctive therapies) on peri-implant and periodontal radiographic outcomes. The objective was to identify the most predictable and reliable treatment modalities by a quantitative comparison of outcomes using meta-analysis.

Materials and methods

Search Strategy

In order to achieve the aims of this study, an electronic literature search was conducted using Ovid MEDLINE, EMBASE and EBM Review – Cochrane Central Register of Control Trials and Cochrane Database of Systematic Reviews. The following keywords were combined: 'Tooth Implantation' OR 'Dental Implants' OR 'Tooth implants' OR 'Oral Implants' OR 'Endosseous implants' OR 'Osseointegrated implants' AND 'Periimplantitis' OR 'Peri-implantitis' OR 'Peri-implant disease' OR 'Peri-implant defect' OR 'Peri-implant infection' OR 'Peri-implant inflammation' OR 'Peri-implant bone loss' AND 'Management' OR 'Treatment' OR 'Therapy' AND 'Surgery' OR 'Surgical' OR 'Surgical approach' OR 'Open flap' OR 'Access flap' OR 'Resective' OR 'Regenerative' OR 'Bone regeneration' OR 'Bone augmentation' (Table 1).

Study Selection Criteria

The criteria for inclusion of specific studies in this review were human studies published in the English language. Studies were selected for randomized controlled trials or prospective cohort studies only with ≥ 10 patients and ≥ 6 months follow-up (the longest follow up period was chosen in longitudinal studies which were published more than once). Experimental animal or studies *in vitro* were excluded.

Primary and secondary outcomes

The primary outcome for this review study was the reduction of BOP in implants treated surgically for peri-implantitis. The secondary outcomes were the assessment of PPD and RBL (radiographic bone loss).

Qualitative assessment methods (Risk of bias)

The modified 'Critical Appraisal Skills Program' (CASP) checklists was used to assess the quality of the studies⁴⁵. The risks of bias were categorized into; low risk (all the criteria were met), moderate risk (1-2 criteria were missed) or high risk (>2 criteria were missed).

Statistical Analysis

Meta-analyses were conducted separately for the parameters PPD and RBL using computer software (Stata® V13). All data used in meta-analysis were those measurements made at the end of the observation period for both control and intervention arms. Forest plots were produced to represent the standardized mean difference (SMD) between control and test groups. Pooled estimates and associated 95% confidence interval (CI) from meta-analysis for each type of intervention were indicated by 'diamond' symbols in Fig. 5; the center of the diamond (with respect to the x-axis) indicates the pooled point estimate and the edges indicate the pooled 95% CI. I-squared values and a chi-squared test were used to assess the heterogeneity of the studies.⁴⁶ Where heterogeneity was not problematic fixed-effects meta-analysis was employed and random-effects meta-analysis was otherwise employed. Although some evidence of an outlier was observed for RBL for some studies^{49,50}, results for this study were included in Forest plots because it was not used to form any 'pooled' estimates (it was the only study in the 'implantoplasty' group).

Results

Literature on peri-implant disease

Initial results highlighted the increase in published research on peri-implant disease over the last 15 years (Fig. 1a). There were significantly more publications on peri-implantitis and its surgical treatment compared to the numbers of publications regarding peri-implant mucositis and non-surgical treatment (Fig. 1b).

Manuscript selection

The literature search identified 320 studies, and 25 were selected for full-text evaluation following title and abstract screening. A further 9 papers were excluded following careful review (Fig. 2), and the remaining 16 studies included and reviewed for detailed qualitative and quantitative assessment (see Supplementary Information for a summary of the included studies). Selection was based on the 'Preferred Reporting Items for Systematic review and Meta-Analysis' flow chart PRISMA ⁴⁸. Of the 16 studies included, 9 were RCTs, 4 were comparative prospective studies, and 3 were single group prospective studies. The CASP checklist revealed that 53% of the included studies have a high risk of bias, 35% have a moderate risk, and the remaining studies (12%) have a low risk of bias. The follow-up periods of the studies that were included in the review ranged from 6 to 60 months. However, the participants were observed for 12 months in most of the studies.

Surgical interventions

The main type of surgical intervention was bone augmentation following mechanical debridement, which was examined in 44% of the studies (Fig. 3a). The effect of mechanical debridement combined with surface decontamination was examined in 38% of the studies. Relatively few studies (12%) considered the effects of mechanical debridement only; 6% of the studies examined mechanical debridement with implantoplasty. Xenograft materials were used for 64% of the bone augmentation cases, whilst autogenous bone was used for 20% of the augmentation studies. CHX was the most common surface decontamination method (57%) and was used in all of the cases (which included debridement plus surface decontamination; Fig. 3b).

Study outcomes

The parameters used in clinical measurement of peri-implantitis were BOP, PPD, and RBL. The majority of studies used both clinical and radiographic outcomes (69%), and the remaining studies

employed clinical parameters only (31%). Three studies^{28, 29, 49} measured change in outcome measurements with time (3, 6, and 12 months follow-up) and they showed that the mean BOP was significantly decreased ($P < 0.05$) after 3 and 6 months followed by a gradual increase from 6 to 12 months (Fig. 4a). The mean PPD was also decreased significantly ($P < 0.05$) at 3-month follow-up then remained relatively constant during the remaining periods (Fig. 4b). By contrast, RBL had not increased significantly ($P > 0.05$) after 3 months.

Meta-analysis

The meta-analysis was conducted using 8 RCTs^{28, 29, 32, 34, 50-53} and 2 controlled prospective cohort studies^{40, 44} as they reported mean reductions (and standard deviations) for PPD and RBL. The forest plots for PPD and RBL are represented by the four methods for surgical peri-implantitis treatment identified: 1) surface decontamination, 2) implantoplasty, 3) bone augmentation, and 4) additional use of membranes in bone regeneration. Few studies have published data relating to BOP, and so no meta-analysis could be conducted for this parameter.

Meta-analysis demonstrated that implants treated with surface decontamination had SMD of -0.21 (95% CI: -1.70 to 1.27) for PPD reduction. Only one study^{50, 51} reported the effect of implantoplasty on PPD reduction which shows a significant SMD of -3.33 (95% CI: -4.37 mm to -2.28 mm). Bone augmentation with grafting materials and the additional use of membrane resulted in SMD of 0.15 mm (95% CI: -0.55 to 0.84 mm) and 0.30 mm (95% CI: -0.31 to 0.91 mm) respectively (Fig. 5a). In terms of RBL changes, the use of surface decontamination methods resulted in SMD of 0.54 mm (95% CI: -0.20 to 1.28 mm). Whereas implant treated with implantoplasty, had SMD of -3.38 (95% CI: -4.43 to -2.33 mm). The SMD for RBL changes after the use of bone augmentation was -1.50 (95% CI: -0.80 to -0.31 mm). However, the additional use of membrane has SMD of -0.16 (95% CI: -0.56 to 0.24 mm) (Fig. 5b). Whilst implantoplasty and bone augmentation resulted in significant improvement in RBL, the use of surface decontamination or additional membrane application failed to significantly affect observed treatment outcomes.

Heterogeneity was found to be small or moderate for the additional membrane subgroup (i.e.: RBL, I-squared = 0.0%, P = 0.64; PPD, I-squared = 52.1%, P = 0.152) and so random-effects meta-analysis should provide a reasonable pooled estimates in this case. Heterogeneity was found to be high for the surface decontamination subgroup (i.e.: RBL, I-squared = 88.6%, P < 0.001; PPD, I-squared = 97.1%, P < 0.001). A sensitivity analysis for RBL and for the additional membrane subgroup could not be carried out for due to the small number of studies in this case. A sensitivity analysis could be carried out for PPD for this subgroup, where removal of the study with the smallest sample size of seventeen subjects in total (namely, Schwartz et al., 2013) did not affect pooled results very greatly (i.e., SMD = -0.253 and 95% CI = -2.001 to 1.494), whereas removal of the only “outlying” study that indicated a positive mean difference (namely, de Waal et al., 2015) did affect pooled results (i.e., SMD = -0.866 and 95% CI = -1.663 to -0.069). This result indicates a significant reduction in PPD for surface decontamination subgroup in this circumstance, although caution should still be exercised due to the small number of studies and heterogeneity. Again, funnel plots are likely to yield limited information only due to the small number of the studies included in the analysis.

Discussion

This systematic review and meta-analysis was conducted to explore the literature relating to the surgical management of peri-implantitis. It was evident that the patient selection criteria for entry into the studies (and the definition of ‘peri-implantitis’) varied considerably between the included studies. For example, one study defined peri-implantitis by implants with RBL indicating >50% of bone loss⁴⁰, whereas other studies defined peri-implantitis as affecting implants that exhibited PPD >6mm with radiographically visible bony defects^{32, 54, 55}.

Radiographic interpretation of results was found to be inconsistent. Defect configuration needs to be taken into account, and this is particularly evident where bone regeneration is to be attempted using guided bone regeneration⁵⁵. Rocuzzo et al. (2016) went on to show that the circumferential defects showed better bone regeneration compared with the other types of defect.

However, another four-year study which included combined surgical therapy, surface decontamination, and implantoplasty revealed that the outcomes were not directly affected by the defect configuration ³².

Plaque control is pivotally important in peri-implant disease and response to treatment ¹⁵. Adequate oral hygiene maintaining plaque scores at lower levels ($PI \leq 1$) was important for reducing the incidence of BOP ⁵⁶. The severity of peri-implantitis at the commencement of treatment (as measured by the PPD and RBL) may clearly influence treatment outcomes ^{35, 57}. Other important plaque-retentive factors, e.g. surface roughness are an important consideration when conducting comparative studies ^{49, 53, 54}. A history of both smoking and periodontitis has been shown to have an adverse effect on the treatment of peri-implantitis ^{44, 52, 58}. Due to the small numbers of patients, variation in tobacco usage, and incomplete assessment of the severity of the previous periodontal disease in the papers included within this study, this correlation could not be linked to the outcomes of surgical peri-implantitis treatment.

The definition of a successful treatment also varied between studies. In marked contrast, some studies ⁴⁹ simply considered the survival of the affected implants following treatment to represent success. Other studies ^{28, 29, 53, 57} have considered no further bone loss and presence of PPD ≤ 5 mm, with no BOP, to be a successful treatment. Inter- and intra-examiner bias may also lead to variable in outcome measures, for example, force of probing ⁵⁹. Furthermore, PPD alone is considered as an invalid marker for the progression of the disease as the reduction in PPD post-treatment may simply reflect gingival recession and/or the surgical technique e.g. apically-repositioned flap procedures ^{52, 60}. Although radiographic assessment is the only truly non-invasive method for measuring marginal bone levels ⁵² it can only indicate 'defect-fill' but not the actual re-osseointegration ⁴⁴ and represents the mesial and distal bone levels only ⁶¹. More recently, cone-beam CT has been used to detect the levels of buccal and lingual bones, although concerns have been raised regarding both radiation exposure and their validity due to a radiolucent halo that may occur around the implant ⁵¹.

The rationale behind the use of adjunctive systemic antibiotics in the management of peri-implantitis was considered in three studies^{40, 49, 58}. There is a lack of evidence to support the prescription of antibiotics in peri-implantitis treatment, which appears operator-dependent. An RCT investigating the effectiveness on systemic antibiotics failed to demonstrate any effect on local microbiological parameters within the defect⁵³.

The most popular surface decontaminant was CHX, which has been tested extensively and approved to have a broad-spectrum anti-bacterial activity⁶². Variation occurred in the CHX concentrations used in two studies (0.12% CHX Vs placebo²⁹ or 2% CHX Vs 0.12%²⁸). Although both studies reported reduced microbial loads when compared to control groups, this did not translate into demonstrable clinical effects on peri-implantitis. Although other chemical antimicrobial treatments were employed e.g. H₂O₂, H₃PO₄, and EDTA, no studies compared their effects to other adjunctive treatments (or placebo-treated control groups). A 4-year review revealed that curette and saline mechanical debridement showed better results than those treated with Er:YAG laser³², although one study indicates that the Er:YAG laser gave better outcomes at 2-year follow-up⁶³. Meta-analysis failed to detect any significant difference in the use of surface decontamination (via CHX or Laser) on PPD and RBL. Previous studies have indicated that treatment results are independent of decontamination method and that other risk factors such as oral hygiene, defect configuration are better predictors of treatment success^{33, 55}.

Implantoplasty reduces the macro-surface texture (threads) of the implants. The authors feel that the procedure is effective, partly as it is associated with complete elimination of the primary aetiological factor in peri-implantitis- namely the biofilm. Barbour et al. (2007) reports that it may increase the micro-surface roughness leading to biofilm retention. Furthermore, it may alter implant strength^{37, 64} and increase the temperature of the implants surface⁶⁵, leading to adverse effects on bone cellularity⁶⁶. The significant improvement of clinical and radiographic parameters following implantoplasty was only based on one study^{50, 51} and further research regarding this method is needed.

Bone augmentation is limited due to the biological principle of bone regeneration which needs a blood supply to provide nutrition, inflammatory cells to induce bone formation (osseinduction), and collagen matrix for osseointegration⁴³. The significant effect of bone augmentation on RBL relates to the bone grafts material occluding the defect; no effect on clinical outcome (PPD) is evident⁵². Autogenous bone particles ± membranes in multi-walled defects resulted in significant improvement in PPD and RBL at 36 months⁴⁰. In contrast, Aghazadeh et al. (2012) demonstrated that bovine-derived xenograft (BDX) was more effective than autogenous particulate bone⁵⁸. Khoury and Buchmann (2001) and Roos-Jansåker et al. (2014) were unable to demonstrate any additional benefits in comparison to defects treated with graft material alone^{40,44}.

There are several limitations of this current study due to the inclusion of English language papers only, as well as considerable variability between the different studies included in this review relating to the inclusion/ exclusion criteria. Furthermore, there were only a small number of studies included for each type of surgical intervention, with most studies consisting of relatively small sample sizes and high risk of selection bias in patient inclusion. The high degree of heterogeneity between studies prevents quantitative comparison between the groups⁴⁷. Therefore, neither the differences between the groups nor the overall results were calculated. Furthermore, the meta-analyses should be interpreted cautiously because of the small number of the included studies in each group and the high degree of heterogeneity between them.

This current review concludes that a need exists for a long-term, double blind RCT with large sample size and split-mouth technique are required to eliminate patient-related bias. In addition, all potential confounders should be taken into account. Finally, it would be helpful if the definition, diagnosis and the outcomes of the disease were standardised, to be able to conduct more precise reviews, meta-analyses and the evidence-based surgical treatment of these patients.

Conclusion

This systematic review shows that a surgical approach to mechanical debridement alone may result in improved clinical outcomes, with no evidence to show the benefits of apically-repositioned flap procedures. No additional clinical benefits were found from the use of surface decontaminants (chemicals or lasers) or additional systemic antibiotics. A single study demonstrated a significant improvement following implantoplasty. Bone augmentation improved radiographic bone levels; the use of additional membrane/s, however, did not result in any additional benefit. The high degree of heterogeneity and the small number of controlled studies make it difficult to identify which procedure is superior to any other.

Funding

None

Conflict of Interest

The authors confirm that there are no conflicts of interest to declare.

Ethical approval

None required

References

1. Berglundh T, Persson L, Klinge B. A systematic review of the incidence of biological and technical complications in implant dentistry reported in prospective longitudinal studies of at least 5 years. *J Clin Periodontol* 2002; 29 Suppl 3: 197-212; 32-3.
2. Gotfredsen K. A 10-year prospective study of single tooth implants placed in the anterior maxilla. *Clin Implant Dent Relat Res* 2012; 14: 80-7.
3. Rosa MB, Albrektsson T, Francischone CE, Francischone CE, Schwartz-Filho HO, Wennerberg A. The influence of surface treatment on the implant roughness pattern. *J Appl Oral Sci* 2012; 20: 550-5.
4. Alzarea BK. Assessment and evaluation of quality of life (OHRQoL) of patients with dental implants using the oral health impact profile (OHIP-14) - a clinical study. *J Clin Diagn Res* 2016; 10: ZC57-60.
5. Jung RE, Zembic A, Pjetursson BE, Zwahlen M, Thoma DS. Systematic review of the survival rate and the incidence of biological, technical, and aesthetic complications of single crowns on implants reported in longitudinal studies with a mean follow-up of 5 years. *Clin Oral Implants Res* 2012; 23 Suppl 6: 2-21.
6. Jung RE, Pjetursson BE, Glauser R, Zembic A, Zwahlen M, Lang NP. A systematic review of the 5-year survival and complication rates of implant-supported single crowns. *Clin Oral Implants Res* 2008; 19: 119-30.
7. Zitzmann NU, Berglundh T. Definition and prevalence of peri-implant diseases. *J Clin Periodontol* 2008; 35: 286-91.
8. Elemek E, Almas K. Peri-implantitis: etiology, diagnosis and treatment: an update. *N Y State Dent J* 2014; 80: 26-32.
9. Atieh MA, Alsabeeha NH, Faggion CM, Duncan WJ. The frequency of peri-implant diseases: a systematic review and meta-analysis. *J Periodontol* 2013; 84: 1586-98.
10. Vervaeke S, Collaert B, Cosyn J, Deschepper E, De Bruyn H. A multifactorial analysis to identify predictors of implant failure and peri-implant bone loss. *Clin Implant Dent Relat Res* 2015; 17 Suppl 1: e298-307.
11. Smeets R, Henningsen A, Jung O, Heiland M, Hammächer C, Stein JM. Definition, etiology, prevention and treatment of peri-implantitis--a review. *Head Face Med* 2014; 10: 34.
12. Roos-Jansåker AM, Renvert H, Lindahl C, Renvert S. Nine- to fourteen-year follow-up of implant treatment. Part III: factors associated with peri-implant lesions. *J Clin Periodontol* 2006; 33: 296-301.

13. Casado PL, Pereira MC, Duarte ME, Granjeiro JM. History of chronic periodontitis is a high risk indicator for peri-implant disease. *Braz Dent J* 2013; 24: 136-41.
14. Linkevicius T, Puisys A, Vindasiute E, Linkeviciene L, Apse P. Does residual cement around implant-supported restorations cause peri-implant disease? A retrospective case analysis. *Clin Oral Implants Res* 2013; 24: 1179-84.
15. Mombelli A, Lang NP. The diagnosis and treatment of peri-implantitis. *Periodontol* 2000 1998; 17: 63-76.
16. Laine ML, Leonhardt A, Roos-Jansåker AM, Peña AS, van Winkelhoff AJ, Winkel EG, Renvert S. IL-1RN gene polymorphism is associated with peri-implantitis. *Clin Oral Implants Res* 2006; 17: 380-5.
17. Renvert S, Roos-Jansåker AM, Lindahl C, Renvert H, Rutger Persson G. Infection at titanium implants with or without a clinical diagnosis of inflammation. *Clin Oral Implants Res* 2007; 18: 509-16.
18. Roos-Jansåker AM, Lindahl C, Renvert H, Renvert S. Nine- to fourteen-year follow-up of implant treatment. Part II: presence of peri-implant lesions. *J Clin Periodontol* 2006; 33: 290-5.
19. Tonetti MS, Chapple IL, Jepsen S, Sanz M. Primary and secondary prevention of periodontal and peri-implant diseases: Introduction to, and objectives of the 11th European Workshop on Periodontology consensus conference. *J Clin Periodontol* 2015; 42 Suppl 16: S1-4.
20. Mombelli A. Etiology, diagnosis, and treatment considerations in peri-implantitis. *Current Opinion in Periodontology* 1997; 4: 127-36.
21. Lang NP, Berglundh T, Heitz-Mayfield LJ, Pjetursson BE, Salvi GE, Sanz M. Consensus statements and recommended clinical procedures regarding implant survival and complications. *Int J Oral Maxillofac Implants* 2004; 19 Suppl: 150-4.
22. Heitz-Mayfield LJ. Diagnosis and management of peri-implant diseases. *Aust Dent J* 2008; 53 Suppl 1: S43-8.
23. Roos-Jansåker AM, Renvert S, Egelberg J. Treatment of peri-implant infections: a literature review. *J Clin Periodontol* 2003; 30: 467-85.
24. Kotsovilis S, Karoussis IK, Trianti M, Fourmouis I. Therapy of peri-implantitis: a systematic review. *J Clin Periodontol* 2008; 35: 621-9.
25. Renvert S, Roos-Jansåker AM, Claffey N. Non-surgical treatment of peri-implant mucositis and peri-implantitis: a literature review. *J Clin Periodontol* 2008; 35: 305-15.

26. Chan HL, Lin GH, Suarez F, MacEachern M, Wang HL. Surgical management of peri-implantitis: a systematic review and meta-analysis of treatment outcomes. *J Periodontol* 2014; 85: 1027-41.
27. Máximo MB, de Mendonça AC, Renata Santos V, Figueiredo LC, Feres M, Duarte PM. Short-term clinical and microbiological evaluations of peri-implant diseases before and after mechanical anti-infective therapies. *Clin Oral Implants Res* 2009; 20: 99-108.
28. de Waal YC, Raghoobar GM, Meijer HJ, Winkel EG, van Winkelhoff AJ. Implant decontamination with 2% chlorhexidine during surgical peri-implantitis treatment: a randomized, double-blind, controlled trial. *Clin Oral Implants Res* 2015; 26: 1015-23.
29. de Waal YC, Raghoobar GM, Huddleston Slater JJ, Meijer HJ, Winkel EG, van Winkelhoff AJ. Implant decontamination during surgical peri-implantitis treatment: a randomized, double-blind, placebo-controlled trial. *J Clin Periodontol* 2013; 40: 186-95.
30. Leonhardt A, Dahlén G, Renvert S. Five-year clinical, microbiological, and radiological outcome following treatment of peri-implantitis in man. *J Periodontol* 2003; 74: 1415-22.
31. Valderrama P, Wilson TG. Detoxification of implant surfaces affected by peri-implant disease: an overview of surgical methods. *Int J Dent* 2013; 2013: 740680.
32. Schwarz F, Hegewald A, John G, Sahm N, Becker J. Four-year follow-up of combined surgical therapy of advanced peri-implantitis evaluating two methods of surface decontamination. *J Clin Periodontol* 2013; 40: 962-7.
33. Papadopoulos CA, Vouros I, Menexes G, Konstantinidis A. The utilization of a diode laser in the surgical treatment of peri-implantitis. A randomized clinical trial. *Clin Oral Investig* 2015; 19: 1851-60.
34. Bombeccari GP, Guzzi G, Gualini F, Gualini S, Santoro F, Spadari F. Photodynamic therapy to treat periimplantitis. *Implant Dent* 2013; 22: 631-8.
35. Serino G, Turri A. Outcome of surgical treatment of peri-implantitis: results from a 2-year prospective clinical study in humans. *Clin Oral Implants Res* 2011; 22: 1214-20.
36. Subramani K, Jung RE, Molenberg A, Hammerle CH. Biofilm on dental implants: a review of the literature. *Int J Oral Maxillofac Implants* 2009; 24: 616-26.
37. Chan HL, Oh WS, Ong HS, Fu JH, Steigmann M, Sierraalta M, et al. Impact of implantoplasty on strength of the implant-abutment complex. *Int J Oral Maxillofac Implants* 2013; 28: 1530-5.

38. Augthun M, Tinschert J, Huber A. *In vitro* studies on the effect of cleaning methods on different implant surfaces. J Periodontol 1998; 69: 857-64.
39. Haas R, Baron M, Dörtbudak O, Watzek G. Lethal photosensitization, autogenous bone, and e-PTFE membrane for the treatment of peri-implantitis: preliminary results. Int J Oral Maxillofac Implants 2000; 15: 374-82.
40. Khoury F, Buchmann R. Surgical therapy of peri-implant disease: a 3-year follow-up study of cases treated with 3 different techniques of bone regeneration. J Periodontol 2001; 72: 1498-508.
41. Schwarz F, Sculean A, Bieling K, Ferrari D, Rothamel D, Becker J. Two-year clinical results following treatment of peri-implantitis lesions using a nanocrystalline hydroxyapatite or a natural bone mineral in combination with a collagen membrane. J Clin Periodontol 2008; 35: 80-7.
42. Wiltfang J, Zernial O, Behrens E, Schlegel A, Warnke PH, Becker ST. Regenerative treatment of peri-implantitis bone defects with a combination of autologous bone and a demineralized xenogenic bone graft: a series of 36 defects. Clin Implant Dent Relat Res 2012; 14: 421-7.
43. Cypher TJ, Grossman JP. Biological principles of bone graft healing. J Foot Ankle Surg 1996; 35: 413-7.
44. Roos-Jansåker AM, Persson GR, Lindahl C, Renvert S. Surgical treatment of peri-implantitis using a bone substitute with or without a resorbable membrane: a 5-year follow-up. J Clin Periodontol 2014; 41: 1108-14.
45. 'Critical Appraisal Skills Program' (CASP) checklists' [CASP].
http://docs.wixstatic.com/ugd/dded87_7e983a320087439e94533f4697aa109c.pdf (May 2016).
46. Higgins JP, Thompson SG, Deeks JJ, Altman DG. Measuring inconsistency in meta-analyses. BMJ 2003; 327: 557-60.
47. Higgins JP, Green S. Cochrane handbook for systematic reviews of interventions (Vol. 5). Chichester: Wiley-Blackwell, 2008.
48. Moher D, Liberati A, Tetzlaff J et al. Preferred reporting items for systematic reviews and meta-analyses: the PRISMA statement. Int J Surg 2010; 8: 336-41.
49. Heitz-Mayfield LJ, Salvi GE, Mombelli A, Faddy M, Lang NP. Anti-infective surgical therapy of peri-implantitis. A 12-month prospective clinical study. Clin Oral Implants Res 2012; 23: 205-10.

50. Romeo E, Ghisolfi M, Murgolo N, Chiapasco M, Lops D, Vogel G. Therapy of peri-implantitis with resective surgery. A 3-year clinical trial on rough screw-shaped oral implants. Part I: clinical outcome. Clin Oral Implants Res 2005; 16: 9-18.
51. Romeo E, Lops D, Chiapasco M, Ghisolfi M, Vogel G. Therapy of peri-implantitis with resective surgery. A 3-year clinical trial on rough screw-shaped oral implants. Part II: radiographic outcome. Clin Oral Implants Res 2007; 18: 179-87.
52. Wohlfahrt JC, Lyngstadaas SP, Rønold HJ, Saxegaard E, Ellingsen JE, Karlsson S, et al. Porous titanium granules in the surgical treatment of peri-implant osseous defects: a randomized clinical trial. Int J Oral Maxillofac Implants 2012; 27: 401-10.
53. Carcuac O, Derks J, Charalampakis G, Abrahamsson I, Wennström J, Berglundh T. Adjunctive systemic and local antimicrobial therapy in the surgical treatment of peri-implantitis: A randomized controlled clinical trial. J Dent Res 2016; 95: 50-7.
54. Rocuzzo M, Bonino F, Bonino L, Dalmaso P. Surgical therapy of peri-implantitis lesions by means of a bovine-derived xenograft: comparative results of a prospective study on two different implant surfaces. J Clin Periodontol 2011; 38: 738-45.
55. Schwarz F, Sahm N, Schwarz K, Becker J. Impact of defect configuration on the clinical outcome following surgical regenerative therapy of peri-implantitis. J Clin Periodontol 2010; 37: 449-55.
56. Lang NP, Nyman SR. Supportive maintenance care for patients with implants and advanced restorative therapy. Periodontol 2000 1994; 4: 119-26.
57. Rocuzzo M, Gaudio L, Lungo M, Dalmaso P. Surgical therapy of single peri-implantitis intrabony defects, by means of deproteinized bovine bone mineral with 10% collagen. J Clin Periodontol 2016; 43: 311-8.
58. Aghazadeh A, Rutger Persson G, Renvert S. A single-centre randomized controlled clinical trial on the adjunct treatment of intra-bony defects with autogenous bone or a xenograft: results after 12 months. J Clin Periodontol 2012; 39: 666-73.
59. Mombelli A, Lang NP. Clinical parameters for the evaluation of dental implants. Periodontol 2000 1994; 4: 81-6.
60. Mombelli A, Mühle T, Brägger U, Lang NP, Bürgin WB. Comparison of periodontal and peri-implant probing by depth-force pattern analysis. Clin Oral Implants Res 1997; 8: 448-54.

- 498 61. Isidor F. Clinical probing and radiographic assessment in relation to the histologic bone level at oral
499 implants in monkeys. Clin Oral Implants Res 1997; 8: 255-64.
- 500 62. Jones CG. Chlorhexidine: is it still the gold standard? Periodontol 2000 1997; 15: 55-62.
- 501 63. Schwarz F, John G, Mainusch S, Sahm N, Becker J. Combined surgical therapy of peri-implantitis
502 evaluating two methods of surface debridement and decontamination. A two-year clinical follow up
503 report. J Clin Periodontol 2012; 39: 789-97.
- 504 64. Gehrke SA, Aramburú Júnior JS, Dedavid BA, Shibli JA. Analysis of implant strength after implantoplasty in
505 three implant-abutment connection designs: an *in vitro* study. Int J Oral Maxillofac Implants 2016; 31:
506 e65-70.
- 507 65. Ramel CF, Lüssi A, Özcan M, Jung RE, Hämmerle CH, Thoma DS. Surface roughness of dental implants and
508 treatment time using six different implantoplasty procedures. Clin Oral Implants Res 2016; 27: 776-81.
- 509 66. de Souza Júnior JM, Oliveira de Souza JG, Pereira Neto AL, Iaculli F, Piattelli A, Bianchini MA. Analysis of
510 effectiveness of different rotational instruments in implantoplasty: an *in vitro* study. Implant Dent 2016;
511 25: 341-7.

512

Dental Implantology	Peri-implant disease	Procedure	Technique
Tooth Implantation	Periimplantitis	Management	Surgery
Dental Implants	Peri-implantitis	Treatment	Surgical
Tooth implants	Peri-implant disease	Therapy	Surgical approach
Oral Implants	Peri-implant defect		Open flap
Endosseous implants	Peri-implant infection		Access flap
Osseointegrated implants	Peri-implant inflammation		Resective
			Regenerative
			Bone regeneration
			Bone augmentation

515

516 **Figure legends:**

517 **Figure 1** Publishing rate of papers on (a) peri-implant disease and (b) peri-implantitis treatment in
518 the period 2001-2015.

519

520 **Figure 2** PRISMA flow chart for study selection.

521

522 **Figure 3** Proportion of (a) surgical intervention investigated and (b) surface decontamination
523 methods used in the included studies.

524

525 **Figure 4** The relationship between observed outcomes and time for (a) BOP and (b) PPD ^{28, 29, 49}.

526

527 **Figure 5** Forest plot for (a) probing pocket depth (PPD) reductions and (b) radiographic bone level
528 (RBL) changes.

529

530

531

532

533

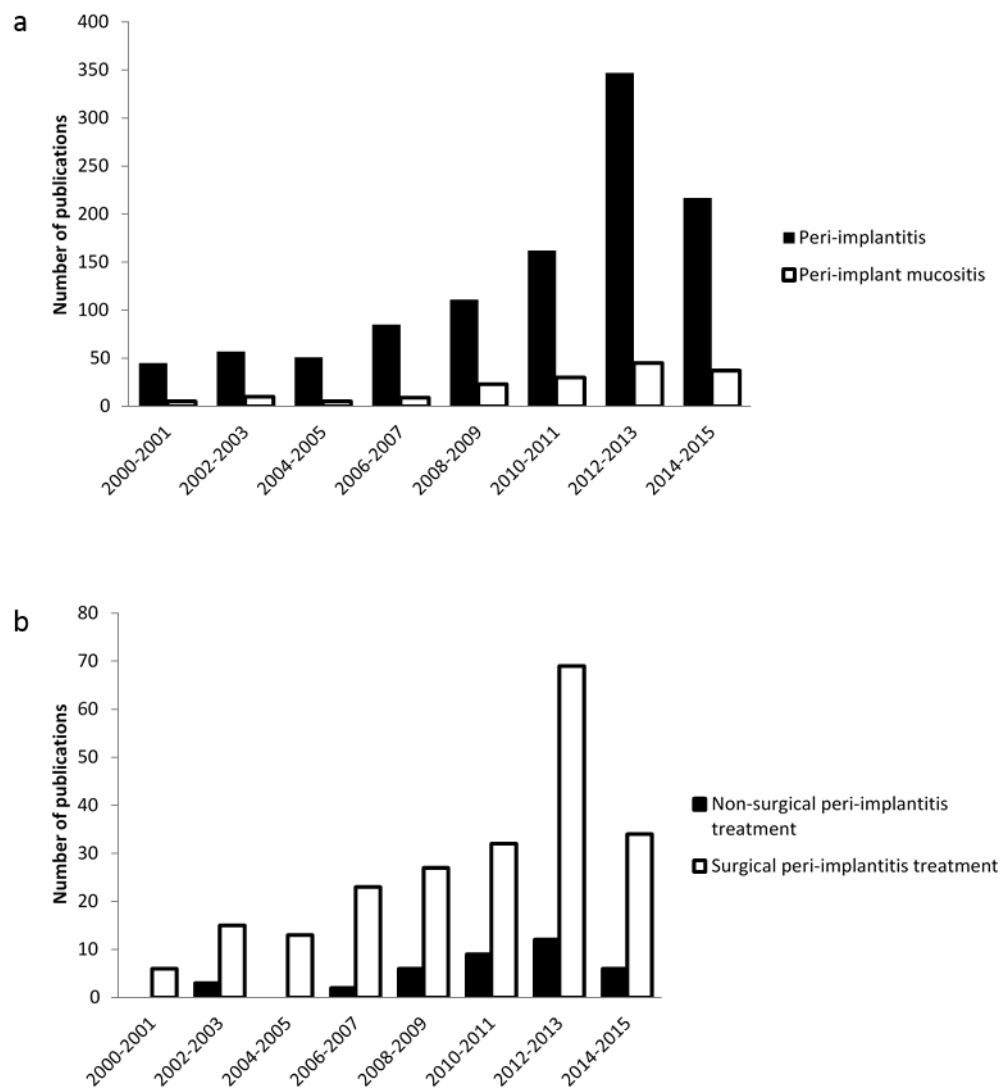
534

535

536

537 Figure 1:

538



539

540

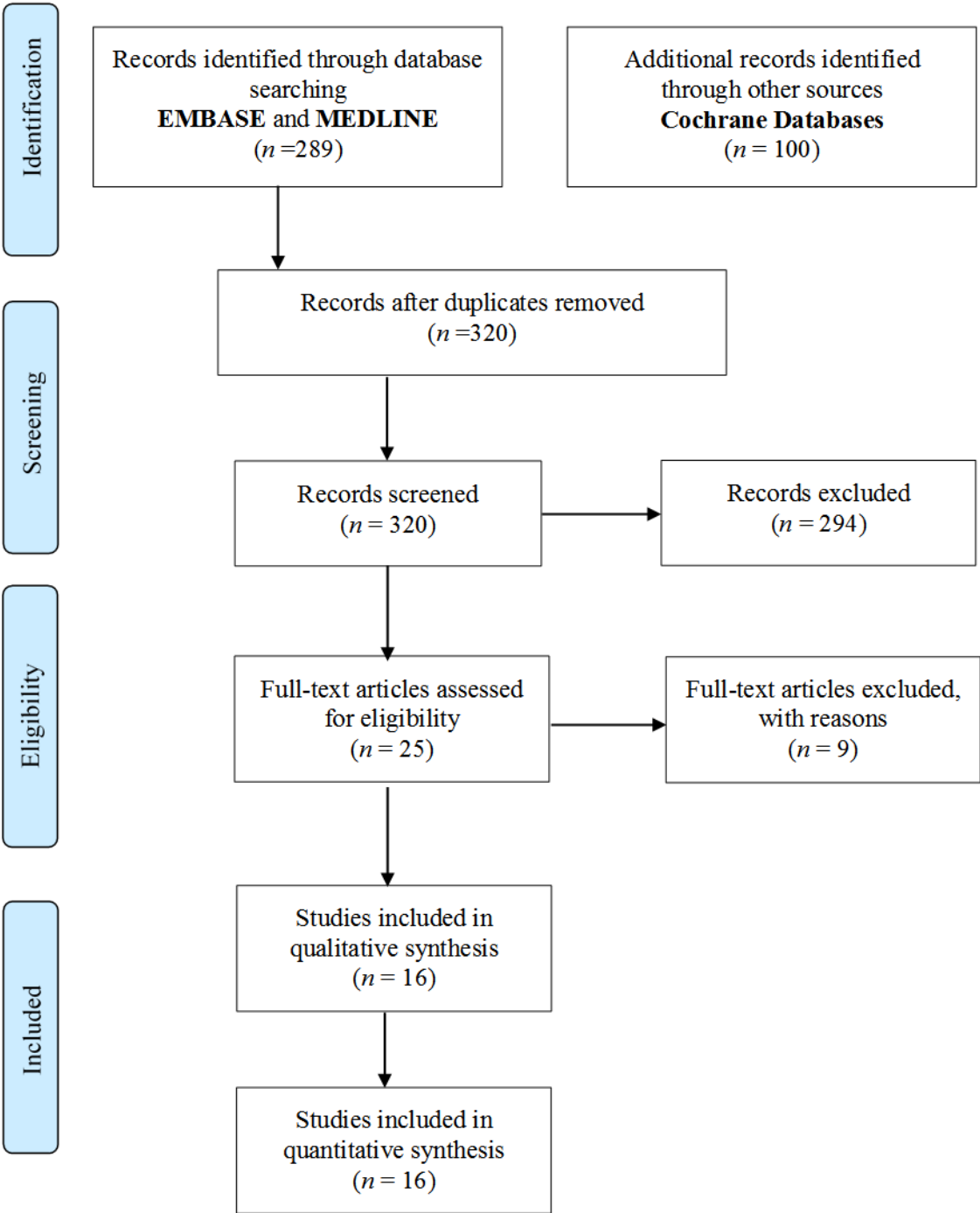
541

542

543

544 Figure 2:

545



546

547

Figure 3:

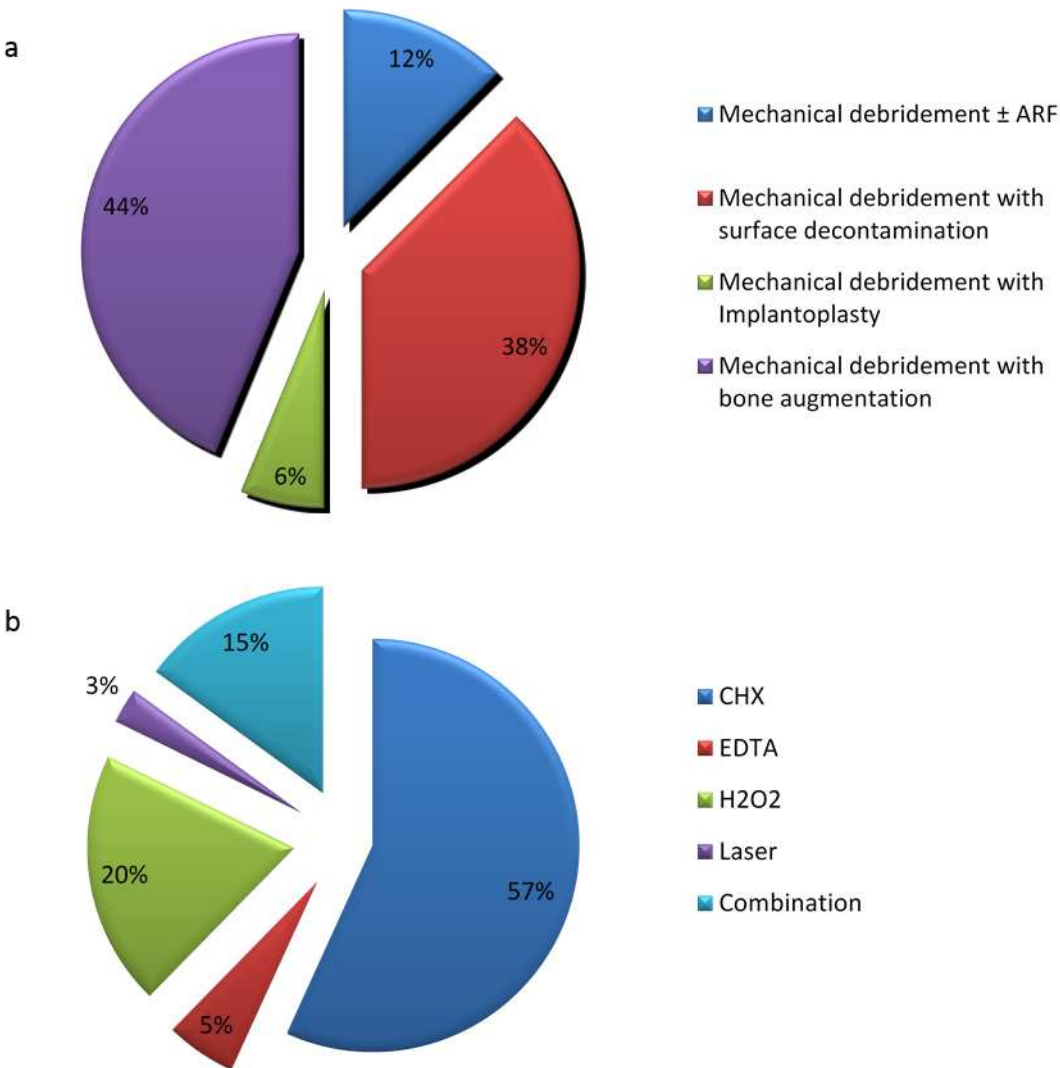
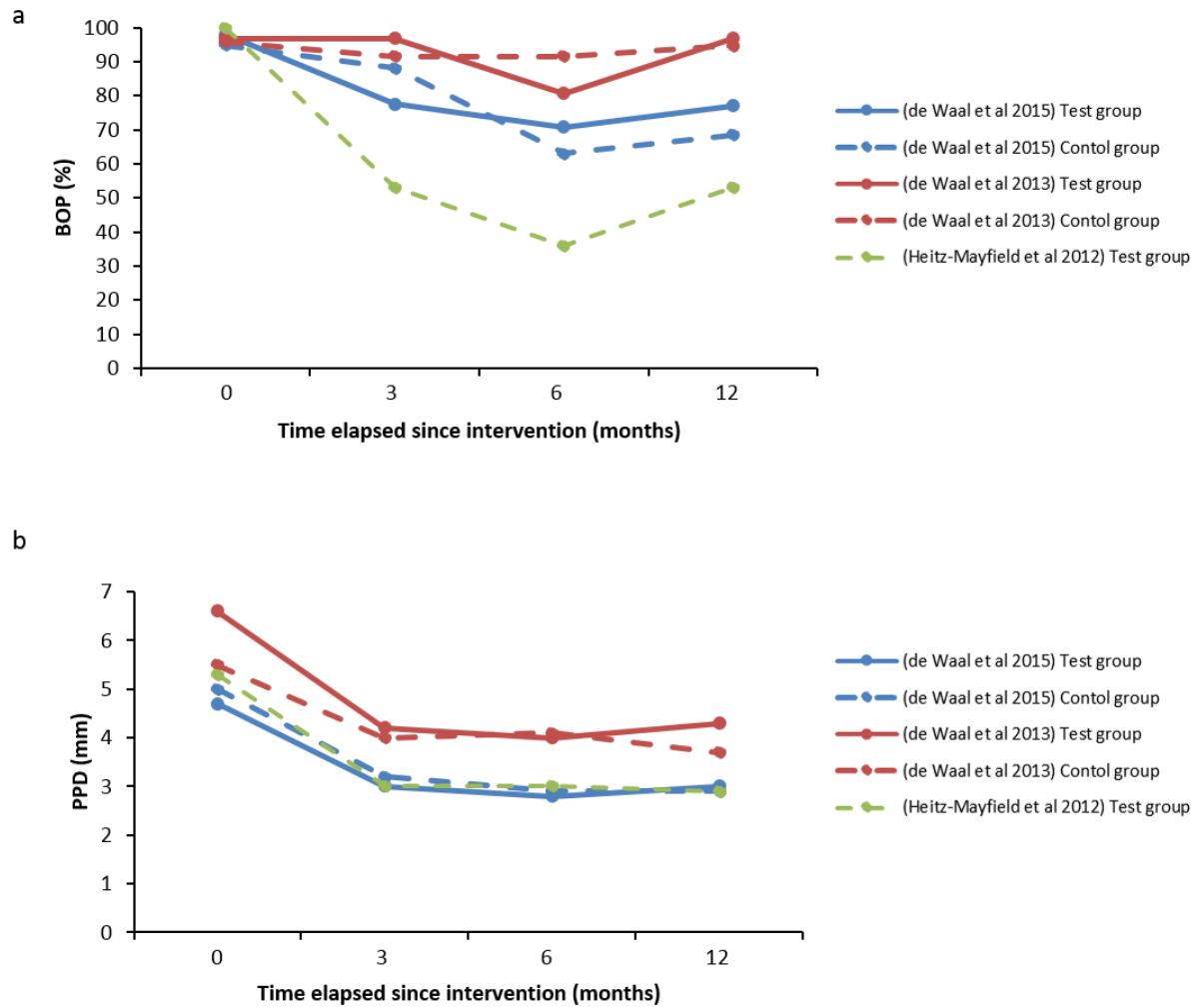
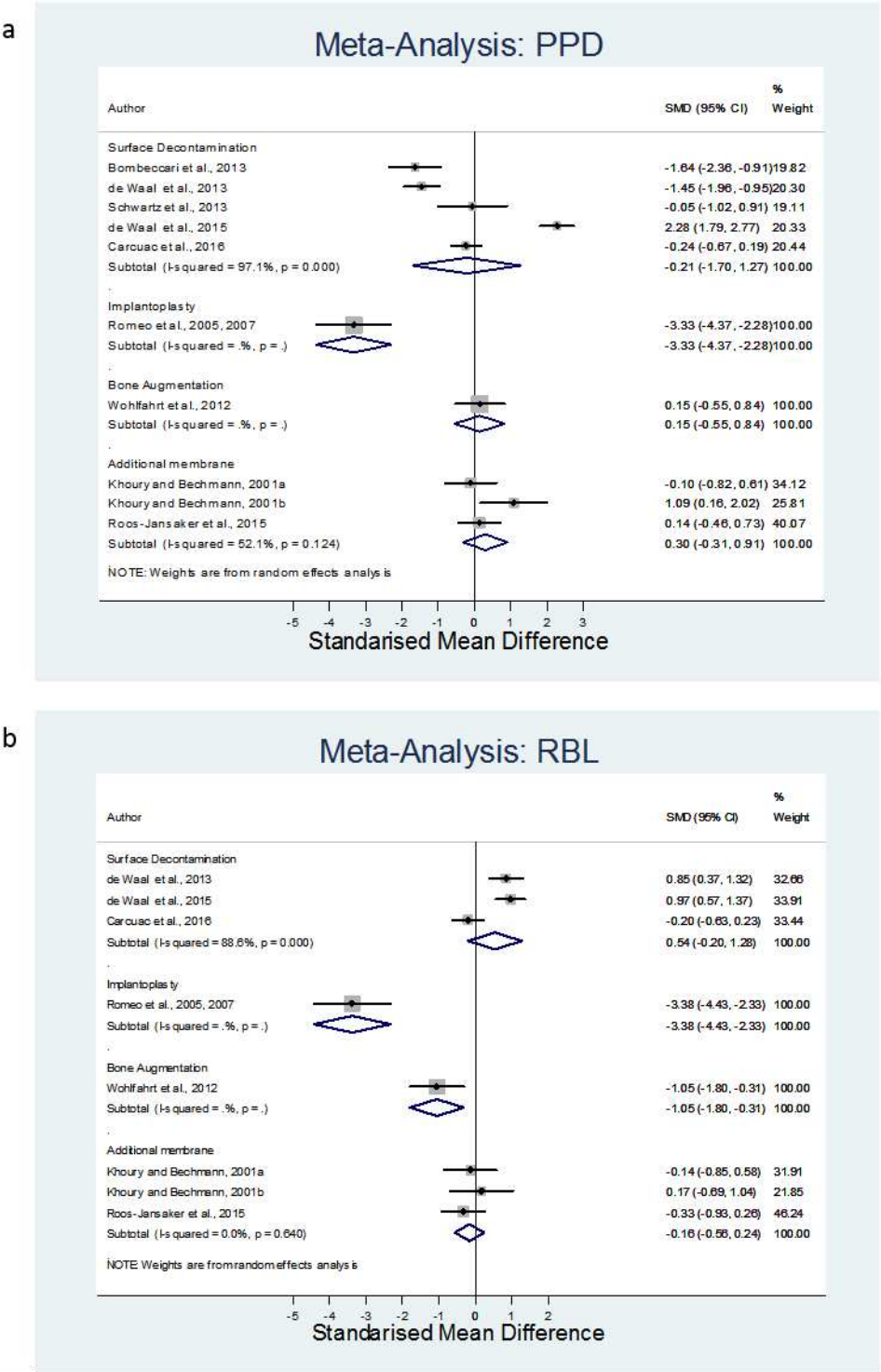


Figure 4:



564 Figure 5:

565



566